UNITED STATES SPECIFICATION

TO ALL WHOM IT MAY CONCERN:

BE IT KNOWN that We, ULRICH J. PFEIFFER and
THORSTEN BURGER, both citizens of Germany, having addresses
of Metzstrasse 34a, D-81667 München, Germany and Speyerer
Str. 8, D-80804 München, Germany, respectively, have invented
certain new and useful improvements in an

APPARATUS FOR DETERMINING CARDIOVASCULAR PARAMETERS

of which the following is a specification.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to an apparatus for determining cardiovascular parameters, in particular an apparatus for the continuous determination of the parameters that characterize a patient's left ventricular pumping action, and an apparatus for the continuous determination of the cardiac volume responsiveness indicator.

2. The Prior Art

It is particularly important to monitor continuously cardiovascular parameters in critically ill patients, for example during surgical procedures performed under total anesthesia, or in case of a critical condition. Of special importance are the parameters that characterize the left ventricular pumping action. It is known from the prior art to determine these parameters by means of pulse contour analysis, for which technical solutions such as the commercially available PiCCO system by Pulsion Medical Systems have been known for some time. With these, the parameters to be determined are calculated from the time curve of an arterially measured pressure. In particular, a

pulse contour analysis based on a non-linear wind kessel model, in which - for example as described in DE 198 14 371 A1 - a non-linear function of the pressure measured close to the aorta is used for the so-called compliance (expandability) of the aorta, usually leads to very useful results. However, in patients receiving mechanical respiration, the validity of the information obtained from such an analysis could sometimes be improved.

Furthermore, in the cardiovascular monitoring of intensive-care patients, it is often of crucial importance to recognize whether a critical cardiac filling state of the patient should be treated by supplying volume or with medication. In particular with patients receiving artificial respiration, this is sometimes difficult, since the state of respiration affects the measured variables. This is briefly explained below.

The mammalian thorax can be regarded as a chamber with a variable volume. The chamber is composed of the partial volumes of the heart, the lungs, the extracardiac vessels, and fixed tissue, such as connective tissue and the esophagus. The thoracic volume changes regularly with

breathing or mechanical respiration. Under
pathophysiological conditions, it may vary due to increased
abdominal pressure, and also due to external pressure, for
example during diving, etc. Looking at a variable thoracic
volume in terms of time, it contains partial volumes which
change very rapidly, for example within seconds, in the
course of a breathing or respiration cycle, as does the gas
volume inside the lungs and the blood volume inside large
vessels and inside the heart, and partial volumes which
change over longer time periods, such as the functional
residual volume of the lungs due to therapeutic intervention,
e.g. application of constant positive end-expiratory
pressure; an increase in extravasal pulmonary fluid (when a
pulmonary oedema is formed), and an increase in pathological
partial volumes (as in case of hematothorax, pneumothorax or
pleural effusion).

It has been known for a long time that there are
interactions between the heart and the lungs during breathing
and in particular during mechanical respiration. In the case
of spontaneous breathing, the inhaled air enters the lungs
due to the negative intrathoracic pressure (ITP) which is
produced by the precordial musculature and the diaphragm.

However, the venous blood flow into the chest region, often called venous reflux, is facilitated during inhalation as well. During exhalation in spontaneous breathing, the intrathoracic pressure becomes positive again, which causes gas to leave the lungs, since the pressure within in the lungs exceeds atmospheric pressure, while the venous reflux is slowed down. The same happens during mechanical respiration when spontaneous breathing is simulated by means of a respirator in the form of an iron lung.

During the most common form of mechanical respiration, i.e. positive-pressure respiration, inhaling is accomplished by producing a positive pressure in the airways of the breathing apparatus outside the lungs. Respiratory gas enters the lungs because the gas pressure inside the lungs is lower. Gas enters the lungs until the pressure in the external airways and the gas pressure in the lungs and internal airways reach an equilibrium. During this inhalation process, the lungs are enlarged, which increases the intrathoracic pressure, and the large blood vessels and the heart itself are compressed. Physiologically, this means that venous reflux is reduced. Exhalation occurs due to the retractive force of the thoracic wall and the lungs

themselves and, to a lesser degree, due to the weight of the thoracic wall itself, whereby the intrathoracic pressure (ITP) drops again while the venous reflux increases.

The above described changes in venous reflux during spontaneous breathing as well as during mechanical positive respiration have a direct effect on the cardiac filling and - via the so-called Frank Starling mechanism - on the ventricular output, i.e. the stroke volume. In simplified terms, the Starling mechanism describes a relationship between the diastolic cardiac filling volume and the cardiac stroke volume. The more the heart is filled in the diastolic phase, the greater is the output of cardiac stroke volume. This relationship is predominantly linear in a normal heart and becomes flatter when a normally contracting heart is overfilled in the diastolic phase. This is shown in Fig. 1, where the left ventricular stroke volume (LVSV) is plotted schematically against the left ventricular end-diastolic volume (LVEDV) which essentially corresponds to the filling status in the diastolic phase. The middle curve shows the normal pattern. When positively inotropic substances such as adrenalin are administered, i.e. when the cardiac contraction force is increased, the Starling curve shifts to the left,

whereas conditions connected with an acutely or chronically changed cardiac contraction force reduce the rise and cause a shift of the curve to the right. The response to a volume increase can be just as varied while the measured end-diastolic volume remains the same.

In the case of spontaneous breathing or mechanical positive respiration, the effects on cardiac filling, especially on the filling of the right ventricle, cause a variable stroke volume of the right ventricle which in turn affects the filling and the output of the left ventricle after perfusion of the lungs. Finally, these changes in cardiac filling can be detected by measuring the periodic fluctuations of the aortic or arterial pressure curve which directly reflect the changes in the left ventricular volume output.

EP 0 666 056 B1 discloses an apparatus for evaluating the necessity of providing instantaneous volume or evaluating how a patient under artificial respiration responds to the intravenous administration of volume substitutes, wherein the systolic pressure variation serves as an indicator of how receptive the patient is to volume.

However, with this apparatus, it is necessary to measure the tidal volume or the respiration pressure of the respirator, and to compare it to the hemodynamic pressure before any conclusions can be drawn. It is not possible to take all interactions between the state of respiration and the measured cardiovascular values into full consideration. Furthermore, the prior art apparatus does not provide any information as to what happens when the patient returns to spontaneous breathing.

SUMMARY OF THE INVENTION

Against the backdrop of the above described problems, the object of the present invention is to create an apparatus for determining parameters that characterize a patient's left ventricular pumping action without lessening the validity of measuring results through the effect of respiration and changing respiratory states. It is also an object of the present invention to create an apparatus for determining a parameter that allows a reliable evaluation of the cardiac volume responsiveness, i.e. of the readiness for a supply of volume even with variable respiration states.

According to one aspect of the invention, this object is achieved by an apparatus for the continuous determination of a parameter characterizing a patient's left ventricular pumping action comprising:

- a first input channel for the continuous recording of a variable physiological first reading directly dependent on the left ventricular pumping action, and

- an evaluation unit for calculating said parameter characterizing the left ventricular pumping action,

wherein the apparatus also comprises a second input channel for the continuous recording of a variable physiological second reading which at least approximately indicates the patient's intrathoracic pressure (ITP) or is dependent on same, and wherein the evaluation unit is programmed for calculating the parameter characterizing the patient's left ventricular pumping action from said first reading, using a corrective function based on said second reading.

According to another aspect of the invention, this object is achieved by an apparatus for the continuous determination of the cardiac volume responsiveness indicator comprising a first input channel for the continuous recording

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of a variable physiological first reading directly dependent on the patient's left ventricular pumping action, a second input channel for the continuous recording of a variable physiological second reading at least approximately representing the patient's intrathoracic pressure (ITP), a third input channel for the continuous recording of a third reading which depends directly on the patient's state of respiration, and an evaluation unit for calculating said cardiac volume responsiveness indicator. The evaluation unit is programmed to use said second and third readings to select a function that can be used for the patient's current state of respiration and based on this function, to calculate sid volume responsiveness indicator from said first and second readings.

The periodic fluctuations of the right or left ventricular stroke volume caused by interaction between heart and lungs, or the measured periodic fluctuations of another physiological signal, which correspond to or reflect the periodic fluctuations of the right or left ventricular output of the stroke volume, such as pressure curves measured in the *Arteria pulmonalis*, the aorta or the arterial tree, or periodic fluctuations of the signal of plethysmographic pulse

oximetry, are used to diagnose the heart's response to changing cardiac filling conditions, i.e. to diagnose the heart's pre-load volume. As described above, these periodic fluctuations, which depend on breathing or artificial respiration, indicate that the heart responds to changes in the cardiac pre-load volume. These fluctuations are caused by the effect of the changing ITP on the volume of the intrathoracic low pressure capacitance system (ITLPCS) consisting of the *Venae cava superior* and *inferior*, the right atrium, the right ventricle in the diastolic phase, the pulmonary vascular system, and the left atrium. The ITLPCS is characterized by a low mean intravascular pressure and a relatively large intravascular volume. In the ITLPCS, the connection between volume and pressure is non-linear, which means that the pressure is very low at a low volume while the mean intravascular pressure increases progressively as the volume increases. In other words, with hypovolemia, changes in ITLPCS volume have little effect on pressure, while with hypervolemia, any change in ITLPCS volume has a great effect on the mean ITLPCS pressure. Any change in the intrathoracic pressure, which is the pressure surrounding the ITLPCS, is transferred directly to the intravascular pressure inside the ITLPCS due to the very high compliance of the vascular

structures contained in the ITLPCS. The transmural pressure
of the ITLPCS can be estimated as the difference between
intravascular pressure and the intrathoracic pressure. The
effective transmural pressure in the ITLPCS determines the
actual vascular dilation and thus the volume within the
ITLPCS.

Hence, a constant breath, such as a mechanical
breath of constant depth, causes the same change in ITP, but
- depending on the volume state of the ITLPCS - it affects
the cardiac pre-load and thus the stroke volume to a varying
degree. The main portion of the ITLPCS consists of the *Venae
cavae superior* and *inferior*, the right atrium and the right
ventricle in the diastolic phase while it is under the lowest
mean intravascular pressure. Therefore, the effects on the
ITP caused by breathing or artificial respiration greatly
influence the right ventricular end-diastolic volume (RVEDV)
and subsequently the right ventricular stroke volume (RVSV),
but they have much less direct influence on the left
ventricular end-diastolic volume (LVEDV) and the left
ventricular stroke volume (LVSV). Over time, however, after
passage through the lungs, these effects on the right
ventricular stroke volume can also be detected in the form of

changes in the left ventricular end-diastolic volume and the left-ventricular stroke volume.

For that reason, the same amount of breathing will have a much greater effect on the development of the left ventricular stroke volume with hypovolemia than with hypervolemia, provided that the left ventricle responds to changes in the pre-load. With the help of the apparatus according to the invention, the totality of these relationships can be used clinically for examining the volume responsiveness of the left ventricle. As a clinical consequence, a patient whose left heart responds to volume, which means that his heart works in a steeper section of its current Starling curve, would be supplied with volume to optimize his cardiac output (CO). On the other hand, the supply of volume would be avoided in a patient whose left heart does not respond to volume, since his heart works in the flat section of its current Starling curve. Instead, one would try to optimize his cardiac output by administering positively inotropic substances to shift his function curve into a steeper form (left shift, see Fig. 1).

This information is very valuable for anesthetists or intensive-care specialists. It can be obtained easily and fully automatically with a monitoring system designed along the principles of the apparatus according to the invention. Such a system continuously supplies the stroke volume or any variable reflecting the stroke volume and provides the information as to which type and phase of breathing or mechanical respiration is predominant or being applied, and how the intrathoracic pressure is affected by this kind of breathing or respiration measure.

This approach has the advantage that the heart/lung interaction used for examining the cardiac volume responsiveness can be standardized for spontaneous breathing as well as for mechanical respiration by measuring the change in intrathoracic pressure it causes, while the individual breath volume does not necessarily have to be standardized and does not have to follow a certain pattern, but may be of any magnitude.

On the other hand, there would not be much sense in trying to standardize values which describe breathing itself, since the degree to which the ITLPCS is influenced depends on

the compliance of the respiratory tract itself, on the compliance of the thoracic wall and on the presence of a space-occupying process with a low time constant such as a pulmonary oedema, pneumothorax, hematothorax or pleural effusion. The tidal volume (= breath volume) and all above named factors contribute to changes in ITP, which directly affects the ITPLCS. For that reason, effects caused by breathing/respiration are best standardized by taking into account the changes in ITP which accompany them. Phase-related changes in ITP can be derived directly from changes in the continuously monitored central venous pressure (CVP) if changes in the thoracic dimensions are recorded at the same time or (applicable only in the case of mechanical positive-pressure respiration) if the timing and the form of mechanical respiration can be derived from the pressure of the respiratory system measured close to the patient, thus avoiding any time lag.

BRIEF DESCRIPTION OF THE DRAWINGS

Other objects and features of the present invention will become apparent from the following detailed description considered in connection with the accompanying drawings. It is to be understood, however, that the drawings are designed

as an illustration only and not as a definition of the limits of the invention.

In the drawings, wherein similar reference characters denote similar elements throughout the several views:

FIG. 1 shows as a background to the invention, a Frank Starling curve and its change due to cardiac stimulation by pharmacological means, and due to cardiac insufficiency;

FIG. 2 shows the basic interaction between different volumes and the intrathoracic pressure;

FIG. 3 shows an apparatus according to the invention being applied to a patient;

FIG. 4a is a schematic representation of the temporal variability (change vs. time) of the readings which determine the calculation of the volume responsiveness indicator in case of positive pressure respiration;

FIG. 4b is a schematic representation of the temporal variability of the readings which determine the calculation of the volume responsiveness indicator in case of spontaneous breathing;

FIG. 5a shows a schematic view of the course of the volume responsiveness indicator depending on the end-diastolic volume with positive pressure respiration; and

FIG. 5b shows a schematic view of the course of the volume responsiveness indicator depending on the end-diastolic volume with spontaneous breathing.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

FIG. 2 shows a schematic view of the volumes affected by or affecting the intrathoracic pressure (ITP) and other characteristic pressures that are of significance in connection with the invention. Inside thoracic wall 1, the ITP acts upon the intrathoracic blood volume (ITBV) which is composed of the above named intrathoracic low-pressure capacitance system (ITLPCS) and the left ventricular end-diastolic volume (LVEDV). Other volumes inside thoracic wall 1 are the gas-filled lung volume L and, if applicable,

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additional volumes K, such as extravascular lung fluid, pleural effusion, hematothorax, etc., which must be regarded as constant during a measuring period. Aortal pressure AP prevails in the aorta 2 while central venous pressure CVP prevails in the central vein 3. In the case of artificial respiration, the airways are subject to external pressure P.

The apparatus 4 shown in FIG. 3, via input channel 5a, continuously monitors the arterial pressure measured by the pressure sensor 6 in an artery 7. Said arterial pressure must be regarded as a reading Pao which at least approximately corresponds to the aortal pressure. In principle, the arterial pressure can be measured in the aorta 2, in its vicinity, or in the arterial tree. A second reading, the central venous pressure (CVP), which is measured by pressure sensor 8 in central vein 2, is provided continuously by apparatus 4 via input channel 5b. The CVP is regarded as a pressure P_{IT} which approximately corresponds to the ITP. The third reading, which is given via input channel 5c, is a parameter Z that reflects the thoracic compliance. Measuring may be performed, for example, with a strain gauge (DMS), but it is also possible to measure another reading

which directly or indirectly represents thoracic compliance in absolute or relative terms.

Typically obtained timing sequences for thoracic dimension Z (upper diagrams) and the central venous pressure (CVP) are shown in FIG. 4a for mechanical positive pressure respiration and in FIG. 4b for spontaneous breathing. The abscissa is the time axis with cardiac pulse cycles as the axis unit.

By means of conventional algorithms of pulse contour analysis, the appropriately programmed apparatus 4 calculates the stroke volume (LVSV) (lower diagrams in FIGS. 4a and 4b) of the left ventricle (LV), the stroke volume variation SVV, and if applicable other desired cardiovascular readings. The transmural pressure is calculated as the relevant pressure, according to the following formula:

$$Ptransmural = Pao - f(C) * PIT$$

The corrective function $f(C)$ is a function of compliance (C) of the arterial system or primarily the aorta 2, where compliance is preferably determined according to a non-linear

wind kessel model, and the corrective function f(C) can, for
example, take the form of

$$f(C) = 1 - \exp(-a * C)$$

with (a) as the adaptation parameter, but which in any case
increases monotonically as the compliance increases and may
assume values between 0 and 1.

A phase shift Ph1 must be taken into consideration
due to the transpulmonary and left ventricular path. As an
alternative to the stroke volume variation SVV, only the
upward (Δup) or downward (Δdown) deviations of the stroke
volume could be taken into consideration. Δup and Δdown may
also be required for calculating other desired cardiovascular
parameters.

The phase shift Ph0 between the beginning of the
rise of the thoracic dimension curve Z, i.e. beginning
thoracic compliance, and the beginning of the rise of the
curve of the central venous pressure CVP indicates whether
mechanical respiration or spontaneous breathing is taking
place. Such a phase shift Ph0 is noticeable only with

spontaneous breathing (FIG. 4b) but not with mechanical positive pressure respiration (FIG. 4a). However, the less distinct phase shift of the local maximums of the curves of thoracic dimension Z and the central venous pressure can also be used as an alternative criterion.

By means of the above explained criterion, it is decided whether the cardiac volume responsiveness indicator (CVRI) should be calculated according to the formula

$$CVRI = k * (SVV / \Delta CVP)$$

for mechanical positive-pressure respiration, or according to the formula

$$CVRI = 1 - m * (\Delta CVP / SVV)$$

for spontaneous breathing, where ΔCVP is the variation of the central venous pressure during a breathing cycle. The curves obtained as a function of the end-diastolic volume EDV are shown in FIG. 5a for positive pressure respiration and in FIG. 5b for spontaneous breathing.

The k, l and m values are adaptation parameters. As a rule, these would be estimated or experimentally determined constants, but suitable adaptation functions can be used as well, for example with the goal being that both functions provide the same value in their application range when the EDV for the patient's cardiac volume responsiveness indicator has the same value.

Monitor 9 provides the calculated CVRI together with the calculated cardiac output (CO), and - if the patient's filling status is unsatisfactory - this CVRI can help the attending physician to decide whether volume must be supplied or medication is preferable.

Accordingly, while only a few embodiments of the present invention have been shown and described, it is obvious that many changes and modifications may be made thereunto without departing from the spirit and scope of the invention.